



# Low prevalence of bronchial asthma and chronic obstructive lung disease among intensive care unit patients with COVID-19

To the Editor,

In a recent article, Li et al reported low prevalence of bronchial asthma (0.9%) among 548 hospitalized patients with COVID-19 and suggested that Th2 immune response in asthmatic patients may counter the inflammation induced by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection.<sup>1</sup> The prevalence of chronic obstructive pulmonary disease (COPD) in the same cohort was also low (3.1%), even among patients with more severe disease (4.8%). In the study from Wuhan, Zhang et al identified no patients with asthma, allergic rhinitis, and atopic dermatitis among 140 hospitalized COVID-19 patients, whereas only two patients (1.4%) had COPD.<sup>2</sup> On the contrary, the prevalence of chronic lung disease (primarily asthma) was 34.6% among 178 hospitalized adult patients with COVID-19 in the United States.<sup>3</sup> However, that data were available only for a small proportion of the hospitalized patients with COVID-19 (approximately 12%), and therefore, the unexpectedly high reported numbers of chronic lung disease prevalence could be overreported or biased by the patients selection. In another US-based study, asthma was documented in 10.5% of 305 hospitalized patients with SARS-CoV-2 infection and COPD in 5.2%.<sup>4</sup>

In a retrospective study, we assessed the prevalence of bronchial asthma and COPD among 1307 intensive care unit (ICU) patients with SARS-CoV-2 pneumonia who required mechanical ventilation. Patients with inconclusive or pending results of polymerase chain reaction for SARS-CoV-2 were included in the study if they presented with severe acute respiratory infection and typical CT findings (bilateral multilobar ground-glass opacification or multifocal consolidative opacities superimposed on ground-glass opacification) and had no other obvious etiology. Medical records were submitted via Internet by the COVID-19 hospitals located in 60 geographic regions across Russia to the Federal Center at the Sechenov University (Moscow) that provided recommendations on the management of patients. The study was approved by the Ethics Committee of the Sechenov University.

Bronchial asthma and COPD were reported by the local physicians in 23 (1.8%) and 41 (3.1%) of 1307 patients, respectively. Among asthmatic patients, there was a female predominance, whereas most patients with COPD were males. Thirty-nine of 64 patients with asthma and COPD (60.9%) were older than 60, and 51 patients (79.7%) had other chronic diseases (Table 1). Despite similar age and occurrence of concomitant diseases, patients with

COPD showed a trend to a more severe course of COVID-19, that is, the higher rates of invasive ventilation and shock, although most differences between the two groups did not reach statistical significance.

It was reasonable to anticipate that patients with chronic respiratory diseases would be vulnerable to a more severe viral infection and development of acute respiratory distress syndrome (ARDS) that can complicate SARS-CoV-2 pneumonia. However, the prevalence of bronchial asthma and COPD in the large cohort of critically ill patients with COVID-19 was low and did not exceed that in the general population. Of note, the prevalence of autoimmune rheumatic diseases, such as rheumatoid arthritis or systemic lupus erythematosus, in the same cohort was also low (1.1%). Our findings indirectly suggest that, unlike cardiovascular diseases or diabetes mellitus, chronic respiratory diseases do not significantly increase the risk of severe COVID-19 requiring admission to ICU for respiratory support. However, COPD (at least milder forms) could have been underreported in our study that prevents us from making any definite conclusions. Of note, a recent meta-analysis of 6 studies in a total of 1558 patients identified COPD as an independent risk factor for progression of SARS-CoV-2 infection.<sup>5</sup>

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) uses angiotensin-converting enzyme-2 (ACE2), a transmembrane protein expressed in the pulmonary and other tissues, as the main entry point into cells and the serine protease TMPRSS2 for viral spike (S) protein priming.<sup>6</sup> Significant reduction in ACE2 expression associated with respiratory allergy and controlled allergen exposures was suggested as a potential mechanism of reduced COVID-19 severity in patients with respiratory allergies.<sup>7</sup> Halpin et al speculated that therapies used by patients with chronic respiratory diseases, for example, inhaled corticosteroids, might at least partly prevent the development of severe SARS-CoV-2 infection.<sup>8</sup> Indeed, administration of inhaled corticosteroids was associated with lower ACE2 or TMPRSS2 genes expression in sputum from asthmatic patients.<sup>9</sup> Both genes expression were similar between patients with asthma and healthy controls. Among asthma patients, male gender, African American race, and history of type 2 diabetes were associated with higher expression of ACE2 and TMPRSS2. Noteworthy, the percentages of African Americans were high in both US-based studies that showed high prevalence of asthma among hospitalized patients with COVID-19.

**TABLE 1** Clinical and demographic characteristics of patients with asthma or COPD

|                             | Asthma (n = 23) | COPD (n = 41) |
|-----------------------------|-----------------|---------------|
| Females, n (%)              | 15 (65.2%)      | 13 (31.7)**   |
| Median age (range), years   | 62 (34-83)      | 66 (42-92)    |
| Older than 60, n (%)        | 14 (60.9)       | 25 (61.0)     |
| Respiratory support, n (%)  |                 |               |
| Oxygen therapy              | 2 (8.7)         | 4 (9.8)       |
| Noninvasive ventilation     | 5 (21.7)        | 2 (4.9)*      |
| Invasive ventilation        | 16 (69.6)       | 35 (85.4)     |
| Shock, n (%)                | 1 (4.3)         | 5 (12.2)      |
| Concomitant diseases, n (%) |                 |               |
| Any chronic disease         | 19 (82.6)       | 32 (78.0)     |
| Arterial hypertension       | 13 (56.5)       | 26 (63.4)     |
| Type 2 diabetes             | 6 (26.1)        | 9 (22.0)      |
| Obesity                     | 6 (26.1)        | 9 (22.0)      |
| Coronary artery disease     | 4 (17.4)        | 3 (7.3)       |
| Malignancy                  | 2 (8.7)         | 3 (7.3)       |
| History of stroke           | 0               | 2 (4.9)       |

Note: Some patients had more than one concomitant disease.

\* $P < .05$ .

\*\* $P < .01$ .

It seems doubtful that inhaled corticosteroids alone or in combination with bronchodilators are able to prevent or to suppress a cytokine release syndrome underlying development of ARDS in COVID-19. On the contrary, the use of certain anti-rheumatic medications may prove beneficial in patients with cytokine storm and may explain the low prevalence of autoimmune rheumatic diseases among patients with virus-induced ARDS. Several anti-rheumatic agents are currently under investigation in patients with SARS-CoV-2 infection, whereas in Russia and other countries tocilizumab is being used off-label to stop progression of respiratory failure despite a lack of evidence.

Asthma is frequently associated with increased numbers of eosinophils that have both pro-inflammatory effects and immunoregulatory/antiviral activity and may therefore alter the course of COVID-19 or contribute to virus-induced lung damage. However, in a recent review, Lindsley et al concluded that there is little indication that eosinophils play a protective or exacerbating role during SARS-CoV-2 infection, although blood eosinopenia may predict more severe disease.<sup>10</sup> In our study, absolute blood eosinophil counts were below  $0.02 \times 10^9/L$  in 85.7% and 66.7% of asthmatic and COPD patients, respectively, and no patient showed blood eosinophilia.

In an uncontrolled study, we could not rule out the contribution of COPD to the more severe outcomes of SARS-CoV-2 infection that was shown in the previous studies. However, patients with bronchial asthma do not seem to be at increased risk of SARS-CoV-2 induced ARDS. Our findings suggest that there is no need to change standard treatment for chronic respiratory diseases

during pandemic of COVID-19. Additional studies are needed to prove this hypothesis.

## KEYWORDS

asthma, COPD, infections

## CONFLICT OF INTEREST

Dr Avdeev, Dr Moiseev, Dr Brovko, Dr Yavorovskiy, Dr Umbetova, Dr Akulkina, Dr Tsareva, Dr Merzhoeva, Dr Gainitdinova, and Dr Fomin have nothing to disclose.

## FUNDING INFORMATION

"Russian Academic Excellence Project 5-100."

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